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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/003,047	01/05/98	VAN OOYEN A	261922003302

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EXAMINER	
ZAGHMOUT,O	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/003,047	Applicant(s) Van OOyen et al.
	Examiner Ousama Zaghmout	Group Art Unit 1649

☒ Responsive to communication(s) filed on *4-9-98, 8-21-98*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1, 19-23, 26-28, 33-36, 38, 39, 41, 42, 44, 45, 47, 48, 50, 51, and 54-60* is/are pending in the application.

Of the above, claim(s) *19-23, 33-35, 38, 41, 44, 47, 50, and 53* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 26-28, 36, 39, 42, 45, 48, 51, and 54-60* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Detailed Action

Claims 1, 19-23, 26-28, 33-36, 38-39, 41-42, 44-45, 47-48, 50-51, 53-60 are pending.

Claims 1, 26-28, 36, 39, 42, 45, 48, 51, 54-60 were elected by the Applicants with traverse in the restriction requirements response which was filed 8/13/98. Claims 19-23, 33-35, 38, 41, 44, 47, 50, 53 are withdrawn from further consideration.

The argument made by the Applicants regarding combining groups I, II, III, and V is acknowledged. However, these groups are drawn to a completely different products with completely different chemical make up and activity. As such, searching for the claims of each invention will be completely different and they are patentability distinct ones from the other. Therefore, the groupings of these inventions into groups I, II, III and V is maintained.

The references listed on the IDS filed 4/9/97 were not available for consideration. The examiner was not able to find them. Once they are available, they will be considered.

Notice of draftsperson's patent drawing review (PTO 948) is enclosed.

Claim 59 is objected for depending on canceled claim.

Claim 60 is objected for depending on non-elected claim.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1st Paragraph

Claims 1, 26-28, 36, 39, 42, 45, 48, 51, 54-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabled for the production of transgenic potato plants that express both alpha-amylase (Bacilllus licheniformis) and glucoamylase (Aspergillus niger), does not reasonably provide enablement for all methods of modifying carbohydrate composition of any transgenic plants that express any DNA sequence of any primary enzyme of interest capable of degrading polysacharides, under conditions conducive whereby said enzyme-encoding DNA sequence is expressed and the carbohydrate composition of said plant or plant organ is modified where the DNA molecule encoding glucanase is of any microbial origin. Furthermore, Applicants claim any transgenic plants that express at least one expression cassette which contains a nucleotide sequence encoding any second microbial

enzyme, in addition of the expression of any glucanase of microbial origin in these transgenic plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The breadth of the claims are not commensurate in scope with the enabling support provided. Applicants broadly claim all methods of modifying carbohydrate composition of any transgenic plants that express any DNA sequence of any primary enzyme of interest capable of degrading polysacharides, under conditions conducive whereby said enzyme-encoding DNA sequence is expressed and the carbohydrate composition of said plant or plant organ is modified where the DNA molecule encoding glucanase is of any microbial origin. Furthermore, Applicants claim any transgenic plants that express at least one expression cassette which contains a nucleotide sequence encoding any second microbial enzyme, in addition of the expression of any glucanase of microbial origin in these transgenic plants. However, in the instant disclosure, applicants provide and explicitly demonstrate only the production of transgenic potato plants that express both alpha-amylase (Bacilllus licheniformis) and glucoamylase (Aspergillus niger). The expression of the claimed DNA molecules in transgenic cells and plants by the applicants is very critical for the enablement of the claimed invention in the light of the fact that the process of transforming plants with individual genes to obtain desired phenotypes is unpredictable. Napoli et al. observed a reversible inhibition of expression of the desired gene, when introduced in sense orientation into a plant, so that the

desired phenotype was not observed (The Plant Cell. 1989. Vol. 2: 278-289. see page 279, Abstract).

Furthermore, it is important to show traits encoded by the transgenes will be maintained in these transgenic cells and plants when they are used in breeding programs. This is important in the light of the fact that traits encoded by some transgenes have been shown to decline/or disappear at a later stage thereafter. Carvalho et al. teach that expression of a transgenic glucanase was silenced in a homozygous transgenic tobacco line (T17). Carvalho et al. further teach that transgenic glucanase mRNA was detected at high level in the homozygous plant during the first 4 weeks of development. Carvalho et al. further teach that after 4 weeks, the mRNA level decreased gradually. In some Nicotiana sylvestris plants transformed with a p35S-chitinase gene the lower leaves showed a high chitinase content, whereas the upper leaves, formed later in development, showed low chitinase content and co-suppression of both the transgenic and the endogenous chitinase gene (Carvalho et al. The EMBO Journal. 1992. Vol. 11: 2595-2602. The 4th paragraph under the Discussion section).

Furthermore, the instant disclosure does not disclose any step on how the mutagenesis, modification, the alteration of the coding sequence around the translation initiation site to accommodate Kozak consensus sequence, or the cloning and sequencing of DNA molecules encoding glucanase of microbial origin will be performed. The instant disclosure fails to teach the factors which are essential for successfully expressing a glucanase gene of microbial origin. Furthermore, modification of the coding sequence to enhance the expression of non-plant gene in plants requires many steps which they have not be addressed in the instant disclosure which

include: changes in the localization of the regions of A+T richness to resemble the plant introns, and the optimization of the potential plant polyadenylation signal sequences, ATTTA sequences to avoid any destabilization of the mRNA in the plant.

Taken together, the instant disclosure lacks the proper and sufficient guidance to enable the claims as set forth. Applicants failed to address many of these important issues which are essential for the enablement of the claimed invention. Taken together, the instant disclosure lacks the proper and sufficient guidance to enable the claims as set forth. Thus it is not readily predictable that the genetic modification specifically disclosed will work with other claimed genes and in any plant species. Thus it is not readily predictable that the genetic modification specifically disclosed will work with other genes or other plants. Applicant has provided no specific guidance as to how to select genes which will give the desired effect or provided guidance with regard to selection of other plants and/or the technique to be used in the modification of these genetic modification of these plants. One wishing to practice the invention is left to proceed through trial-and-error to see what will work and what will not.

In view of the breadth of the claims, unpredictability, lack of guidance in the specification of the results as stated above, it is the examiner's position that one skilled in the art to which it pertains, or with which it is most nearly connected, could not practice the invention commensurate in scope with these claims without undue experimentations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 26-28, 36, 39, 42, 45, 48, 51, 54-58 are rejected under 35 U.S.C 103 (a) as being unpatentable over Lawson et al (Biotechnology. 1990 Feb 8:2 127-134), Doi et al (Journal of Bacteriology. 1986. 168: 1272-1276), and Robson et al (Journal of Bacteriology. 1986. Vol. 165: 612-619) in view of Castresana et al (Plant Cell. 1990. Vol. 12: 1131-1143).

Claims are directed to any method of modifying carbohydrate composition of any transgenic plants that expresses any DNA sequence of any primary enzyme of interest capable of degrading polysacharides, under conditions conducive whereby said enzyme-encoding DNA sequence is expressed and the carbohydrate composition of said plant or plant organ is modified where the DNA molecule encoding glucanase is of any microbial origin. Furthermore, Applicants claim any transgenic plants that express at least one expression cassette which contains a nucleotide sequence encoding any second microbial enzyme, in addition of the expression of any glucanase of microbial origin in these transgenic plants.

Lawson et al teach the transformation of a major commercial cultivar of potato, Russet Burbank, with the coat protein genes of PVX and PVY. Lawson et al teach that transgenic plants have expressed both coat protein (CP) genes were resistant to infection by PVX and PVY by mechanical inoculation. One line was also resistant when PVY was inoculated with viruliferous green peach aphids. These experiments demonstrate that CP protection is effective against mixed infection by two different viruses and against mechanical and aphid transmission of PVY (abstract). Lawson et l teach the use of constitutively expressing promoter in transforming potato (Material and Methods).

Lawson et al do not teach or expressly disclose the production of transgenic potato plants with beta-1,3-glucanase or beta-1,4-glucanse nucleotide sequences.

Doi et al teach the cloning and expression in Escherichia coli of the gene for an Arthrobacter beta-(1----3)-glucanase (microbial origin). When inserted in the correct orientation at the BamHI site of plasmid YRp7, an 8.6-kilobase BamHI fragment of Arthrobacter sp. strain YCWD3 DNA gave Escherichia coli HB101 cells harboring the recombinant plasmid pBX20 the ability to lyse bakers' yeast cell walls or bakers' yeast glucan in agar medium. An extract of the transformed E. coli cells contained an endo-beta-(1----3)-glucanase with the same activity pattern as that of glucanase Iroduced by Arthrobacter sp. strain YCWD3. Although part of the glucanase activity was contributed by apparently defective molecules, two protein species were found which had high lytic activity on yeast cell walls and adsorbed to microcrystalline cellulose, and both had a single constituent polypeptide with a molecular weight of about 55,000, as determined by

sodium dodecyl sulfate-polyacrylamide gel electrophoresis. In these properties the protein species were indistinguishable from those glucanase I protein species of Arthrobacter sp. strain YCWD3 which we believe are nearly the intact molecule. Doi et la teach that the cloned fragment of Arthrobacter sp. strain YCWD3 DNA contains the structural gene for glucanase I. A recombinant plasmid obtained by subcloning a PstI fragment of pBX20 into pBR322 caused the transformed E. coli cells to produce apparently defective glucanase molecules only (lines 6-11, page 1272).

Roboson et al teach the cloning of the Bacillus subtilis DLG beta-1,4-glucanase gene and its expression in Escherichia coli and B. subtilis. The gene encoding beta-1,4-glucanase in Bacillus subtilis DLG was cloned into both Escherichia coli C600SF8 and B. subtilis PSL1, which does not naturally produce beta-1,4-glucanase, with the shuttle vector pPL1202. This enzyme is capable of degrading both carboxymethyl cellulose and trinitrophenyl carboxymethyl cellulose. The beta-1,4-glucanase gene was localized to a 2-kilobase (kb) EcoRI-HindIII fragment contained within a 3-kb EcoRI chromosomal DNA fragment of B. subtilis DLG. Recombinant plasmids pLG4000, pLG4001a, pLG4001b, and pLG4002, carrying this 2-kb DNA fragment, were stably maintained in both hosts, and the beta-1,4-glucanase gene was expressed in both (lines 6-13, page 612).

Castresana et al teach the tissue-specific and pathogen-induced regulation of a Nicotiana plumbaginifolia beta-1,3-glucanase gene (gn1). Castresana et al teach the expression of gn1 in Escherichia coli and determined directly that the encoded protein does, indeed, correspond to a beta-1,3-glucanase. In N. plumbaginifolia, gn1 was found to be expressed in roots and older

leaves. Transgenic tobacco plants containing the 5'-noncoding region of gn1 fused to the beta-glucuronidase (GUS) reporter gene also showed maximum levels of GUS activity in roots and older leaves. No detectable activity was present in the upper part of the transgenic plants with the exception of stem cells at the bases of merging shoots. The expression conferred by the gn1 promoter was differentially induced in response to specific plant stress treatments. Studies of three plant-bacteria interactions showed high levels of GUS activity when infection resulted in a hypersensitive reaction. Increased gene expression was confined to cells surrounding the necrotic lesions. The observed expression pattern suggests that the characterized beta-1,3-glucanase plays a role both in plant development and in the defense response against pathogen infection (lines 5-15, page 1131)..

At the time of the invention, it would have been obvious to a person of ordinary skill in the art to produce the claimed transgenic plants as taught by Lawson et al., and any of the genes that are capable of degrading polysaccharides taught by Doi et al and Robson et al for the purpose of enhancing the defense response against pathogen infection. The expression of heterologous genes is well known in the art of plant genetic engineering. One of ordinary skill in the art would recognize that a plant transformed with any of the glucanase genes , in sense orientation, would result in a plant with enhanced resistance against pathogen attack as taught by Castresana et al. Given the value of transgenic plants with enhanced level of resistance against pathogens, as taught by Castresana et al., one would have been motivated to use the method of transformation of Lawson et al in order to practice the instant invention in transgenic plants such as potato. Thus claims 1, 26-28, 36, 39, 42, 45, 48, 51, 54-58 are rejected as they are not

patentable over Lawson et al, Doi et al, and Robson et al in view of Castresana et al. The use of genes which encode a second microbial enzymes (claimed in claim 48) or the leader sequence (claim 39) is a matter of choice unless proof of criticality is provided. Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in absence of evidence to the contrary.

Conclusion

No claims are allowed.

Future Correspondence

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Ousama M-Faiz Zaghmout whose telephone number is (703) 308-9438. The Examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Douglas Robinson, can be reached on (703) 308-2897. The fax phone number for the group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to THE MATRIX CUSTOMER SERVICE CENTER whose telephone number is (703) 308-0196.

Ousama M-Faiz Zaghmout Ph.D.

November 20, 1998

Douglas W. Robinson
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